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10/033,629	12/28/2001	Richard J. Deckelbaum	0575/61238-A/JPW/BJA	9269

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Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/033,629	Applicant(s) DECKELBAUM ET AL.	
	Examiner Ruth A. Davis	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *12-14,18-23,26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,15-17,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1 – 11, 15 – 17 and 24 – 25 in Paper No. 6 is acknowledged. The traversal is on the ground(s) that there is not a serious burden on the examiner and that since the inventions are not independent, restriction is improper. This is not found persuasive because as stated in the previous office action, the inventions are independent and distinct because they have acquired a separate status in the art as a separate subject for inventive effect and require independent searches (as indicated by the different classification). The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 3, 9, 15 – 17 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 9, 15 and their dependents are drawn to an emulsion however are rendered vague and indefinite for reciting "preferentially effects" because it is unclear if the limitations following the phrase are intended to be merely exemplary of the remainder of the claim, and therefore not required, or if the limitations are a required feature of the claims.

The claims are further indefinite because it is unclear what effects are occurring. For example, is the triglyceride increasing or decreasing delivery of the pharmaceutical agent.

Claim 25 is rendered indefinite because it depends on a non-elected claim. Applicant may prefer to change the dependency of claim 25 to claim 24.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1 – 9, 11 and 24 – 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Treskova et al. (September 1999).

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride and the composition is delivered to extrahepatic tissue, and the omega 3 triglyceride effects delivery of the pharmaceutical agent. Applicant additionally claims an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier wherein the ratio of medium to long chain triglycerides is about 1 to 1, by weight. Applicant claims an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the ratio of medium chain to long chain triglycerides to fish oil is about 5 to 4 to 1 by weight. The fish oil is an omega 3 triglyceride and the composition is delivered to an extrahepatic tissue and the omega 3 triglyceride effects delivery of the pharmaceutical agent to the tissue. The compositions have 80% of the particles with a diameter of 150 – 350 nm. Finally applicant claims an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions comprising emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). The emulsions have a 1:1 ratio of medium to long chain triglycerides, and a 5:4:1 ratio of LCT:MCT:omega 3 triglycerides (fish oil) (abstract, p.254). Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract).

The reference anticipates the claimed subject matter.

6. Claims 1 – 2, 4 – 6, 8 and 24 – 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Pscherer et al. (US 6008248).

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega 3 triglyceride. Applicant claims an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier wherein the medium chain to long chain triglycerides are in a ratio of about 1 to 1, by weight. Applicant claims an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the fish oil is an omega 3 triglyceride. Applicant claims an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Pscherer teaches lipid emulsions comprising MCT, LCT, omega 3 triglycerides in the form of fish oil, emulsifiers and vitamin E (a pharmaceutical agent) (col.2 – 4). Specifically, the composition contains 30 – 60% MCT, 40 – 85% LCT (combined vegetable and fish oils) (col.2 line 62-col.3 line7), and 0.6 – 1.5% emulsifiers (col.4 line 20-25), and has particles sizes of less than 0.5 micrometers (col.5 line 6-7).

Although Pscherer does not teach the component amounts are predetermined to delivery pharmaceutical agents to predetermined tissues, the compositions appear to be the same. Therefore the reference anticipates the claimed subject matter.

7. Claims 1 – 2, 10 – 11 and 24 – 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Wretlind et al. (US 4970209).

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega 3 triglyceride. The composition has 80% of the particles with a diameter of 30 – 150 or 150 – 350 nm. Applicant additionally claims an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Wretlind teaches emulsion compositions for delivering therapeutics (abstract), the composition comprising fish oil, emulsifiers, pharmaceutical agents and LCT with particle sizes of 0.005 – 0.5 microns (5 – 500 nm) (col.4).

Since fish oil intrinsically contains omega 3 triglycerides, the reference anticipates the claimed subject matter.

8. Claims 1 – 2, 4, 6 – 8 and 24 – 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Boll et al. (DE 390.057 A).

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega 3 triglyceride. Applicant claims an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier. Applicant claims an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the fish oil is an omega 3 triglyceride. Applicant claims an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Boll teaches lipid emulsions containing omega 3 fatty acids as fish oil, an emulsifier, MCT and tocopherols (a pharmaceutical agent) for endotracheal treatment (abstract).

Although Boll does not teach the component amounts are predetermined to delivery pharmaceutical agents to predetermined tissues, the composition is disclosed for endotracheal treatment. Also, the compositions appear to be the same. Therefore the reference anticipates the claimed subject matter.

9. Claims 1 – 2 and 24 – 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamazaki et al (JP 62 129216).

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier, wherein the fish oil is an omega 3 triglyceride. Applicant claims an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Hamazaki teaches emulsion compositions comprising EPA (LCT) in the form of fish oil and an emulsifier (abstract).

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1 – 11 and 24 – 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Treskova.

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride and the composition is delivered to extrahepatic tissue, and the omega 3 triglyceride effects delivery of the pharmaceutical agent. Applicant additionally claims an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long chain triglyceride and an emulsifier wherein the ratio of medium to long chain triglycerides is about 1 to 1, by weight. Applicant claims an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the ratio of medium chain to long chain triglycerides to fish oil is about 5 to 4 to 1 by weight. The fish oil is an omega 3 triglyceride and the composition is delivered to an extrahepatic tissue and the omega 3 triglyceride effects delivery of the pharmaceutical agent to the tissue. The compositions have 80% of the particles with a diameter of 30 – 150 or 150 – 350 nm. Finally applicant claims an

emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions comprising emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). The emulsions have a 1:1 ratio of medium to long chain triglycerides, and a 5:4:1 ratio of LCT:MCT:omega 3 triglycerides (fish oil) (abstract, p.254). Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract).

Althouh Treskova does not teach the emulsions with particle sizes of 30 – 150 nm, it would have been well within the purview of one of ordinary skill in the art to optimize particle size as a matter of routine experimentation (see other cited references for support). Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the emulsion particle size of Treskova with a reasonable expectation for successfully obtaining an effective emulsion composition.

13. Claims 1 – 11, 15 – 17 and 24 – 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Treskova and Counsell et al. (US 5985941).

Applicant claims an emulsion comprising a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride and the composition is delivered to extrahepatic tissue, and the omega 3 triglyceride effects delivery of the pharmaceutical agent. Applicant additionally claims an emulsion comprising a pharmaceutical agent, a medium chain triglyceride, a long

chain triglyceride and an emulsifier wherein the ratio of medium to long chain triglycerides is about 1 to 1, by weight. Applicant claims an emulsion comprising a pharmaceutical agent, a fish oil, a medium chain triglyceride, a long chain triglyceride, and an emulsifier wherein the ratio of medium chain to long chain triglycerides to fish oil is about 5 to 4 to 1 by weight. The fish oil is an omega 3 triglyceride and the composition is delivered to an extrahepatic tissue and the omega 3 triglyceride effects delivery of the pharmaceutical agent to the tissue. The compositions have 80% of the particles with a diameter of 30 – 150 or 150 – 350 nm. Applicant claims an emulsion comprising a pharmaceutical agent, triglyceride, emulsifier and ligand, wherein the triglyceride delivers the pharmaceutical agent to a tissue, and the ligand effects delivery of the agent. The ligand is apolipoprotein E, specifically human apolipoprotein E or homologs thereof differing by less that 3 amino acids and having activity of human apolipoprotein E. Finally applicant claims an emulsion comprising a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions comprising emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). The emulsions have a 1:1 ratio of medium to long chain triglycerides, and a 5:4:1 ratio of LCT:MCT:omega 3 triglycerides (fish oil) (abstract, p.254). Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract).

Counsell teaches emulsions for hepatic tissue selective delivery of pharmaceuticals (abstract), comprising a lipophilic core and emulsifier (col.5 line 50-59). The core may contain

LCT and fish oils (col.5 line 66 – col.6 line 9, col.11), and the emulsion particle size is 50 – 200 nm (abstract).

The above references do not specifically teach the emulsions comprising the ligand apolipoprotein E, or homologs thereof. However, Treskova does suggest that uptake of the triglycerides are increased in the presence of apolipoprotein E (p.257). In addition, Counsell teaches that the emulsion must associate with apolipoprotein E to make it hepatocyte specific (col.4-5). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by the teachings of Treskova and Counsell to include apolipoprotein E, or homologs thereof, in the disclosed compositions for it's specificity to hepatic and extrahepatic tissues, and for the disclosed effect of increasing triglyceride uptake. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Treskova and Counsell to include apoplipoprotein E or homologs thereof in the compositions with a reasonable expectation for successfully obtaining an emulsion for delivering an agent to extrahepatic tissue.

LEON B. LANKFORD, JR.
PRIMARY EXAMINER

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
June 12, 2003